

## CLAIMS

1. – 52. (CANCEL)

53. (NEW) A method of estimating arterial delay and arterial dispersion ( $t$ ,  $\alpha$ ,  $\sigma$ ) values for outputting blood perfusion indices for a region of interest (ROI) by operating a computer program on intensity data in a computer comprising:

- a. applying a first gamma-variate function (GVF) to an arterial input function ( $AIF_a$ ) to provide an estimated first model of a vascular transport function

$$h_a(t), \text{ wherein for } t < t_1, h_a(t) = 0 \text{ and for } t \geq t_1, h_a(t) = \frac{1}{\sigma_1} (t - t_1)^{\alpha_1} e^{-(t-t_1)/\sigma_1},$$

wherein an estimated  $t_1$  is the transit time of a contrast agent from a measured initial said  $AIF_a$  to a region of interest (ROI);

- b. estimating an initial value  $\sigma_1$  of said contrast agent, wherein said  $\sigma_1 = (t_1)(\beta_1)/(1-\beta_1)$ , wherein said  $\beta_1$  is a known relative dispersion value having a range from 0 to 1;

- c. convolving  $AIF_a(t)$  with said  $h_a(t, \alpha_1=0)$  for obtaining an arterial input function  $AIF_t(t) = AIF_a(t) \otimes h_a(t, \alpha_1=0)$  at said ROI;

- d. estimating a blood flow rate  $F_t$  and a tissue impulse residue function  $R_e(t)$  by deconvolving a concentration curve  $C(t) = (F_t/k_H)AIF_t(t) \otimes R_e(t)$ , wherein  $k_H$  is a hemocrit correction constant having a known value; and

- e. outputting estimated and optimized tissue mean transit time and dispersion ( $t_2$ ,  $\alpha_2$ ,  $\sigma_2$ ) values from an estimated transport function  $h_e(t)$  for input to a simulated transport function  $h_s(t)$ , wherein a simulated tissue impulse residue function  $R_s(t)$  is determined, wherein a simulated concentration curve  $C_s(t)$  is

fitted to said measured  $C(t)$  and quantitative said blood perfusion indices are calculated.

54. (NEW) The method of claim 53, wherein said intensity data is generated by  
5 administering a contrast agent to a body lumen of a body during a dynamic  
imaging scan, wherein said body lumen comprises an artery or vein, wherein  
an image response from said contrast agent is recorded to computer data  
storage in a computer.

10 55. (NEW) The method of claim 53, wherein said  $C(t)$  is a temporal concentration  
of said contrast agent obtained from said intensity data, wherein said intensity  
data comprises contrast images sequentially acquired from a region in a body,  
whereby said contrast agent concentration is plotted versus time.

15 56. (NEW) The method of claim 53, wherein said  $AIF_a$  is based on a measured  
early arrival contrast agent peak intensity from a feeding blood vessel to said  
ROI.

20 57. (NEW) The method of claim 53, wherein said  $AIF_a$  is scaled upward according  
to a venous input function (VIF), wherein said VIF is based on a measured late  
arrival contrast agent peak intensity from a large vein draining from said ROI.

58. (NEW) The method of claim 53, wherein said estimated transit time  $t_1$  is the

transit time of said contrast agent from a measured initial said AIF<sub>a</sub> of said contrast agent C(t) in a body lumen to said ROI, wherein said t<sub>1</sub> is estimated from plots of said AIF<sub>a</sub> versus time and said C(t) versus time.

5 59. (NEW) The method of claim 53, wherein said h<sub>a</sub>(t) is calculated using said estimated transit time t<sub>1</sub> and said estimated dispersion value σ<sub>1</sub>, wherein h<sub>a</sub>(t, α<sub>1</sub>=0) is plotted versus time.

10 60. (NEW) The method of claim 53, wherein said estimated transport function h<sub>e</sub>(t) is calculated using the relation h<sub>e</sub>(t) = - dR<sub>e</sub>(t)/dt.

15 61. (NEW) The method of claim 53, wherein said tissue mean transit time and dispersion (t<sub>2</sub>, α<sub>2</sub>, σ<sub>2</sub>) values are estimated from said estimated transport function h<sub>e</sub>(t), wherein said t<sub>2</sub>, said σ<sub>2</sub> and said α<sub>2</sub> are input to a simulated transport function h<sub>s</sub>(t), wherein said h<sub>s</sub>(t) is said second gamma-variate function.

20 62. (NEW) The method of claim 53, wherein said simulated tissue impulse resistive function R<sub>s</sub>(t) is determined using the relation  $R_s(t) = 1 - \int_0^t h_s(\tau) d\tau$ .

63. (NEW) The method of claim 53, wherein said simulated concentration curve C<sub>s</sub>(t) is determined using the relation C<sub>s</sub>(t) = (F<sub>i</sub>/k<sub>H</sub>)AIF<sub>i</sub>(t) ⊗ R<sub>e</sub>(t) = (F<sub>v</sub>/k<sub>H</sub>)

$$\int_0^t \text{AIF}_i(t) R_i(t-\tau) d\tau.$$

64. (NEW) The method of claim 53, wherein said  $F_t$ , said  $t_1$ , said  $\sigma_1$ , said  $\alpha_2$ , said  $t_2$ , said  $\alpha_2$ , and said  $\sigma_2$  are optimized by a least squares method to fit said  $C_s(t)$  to said  $C(t)$ .

65. (NEW) The method of claim 53, wherein said perfusion indices have the relations:

- a. blood flow (BF) =  $F_t$ ;
- b. Mean Transit Time (MTT) =  $t_2 + \sigma_2(1+\alpha_2)$ ;
- c. Blood Volume (BV) = BF \* MTT;
- d. Arterial Delay (DT) =  $t_1 + \sigma_1(1+\alpha_1)$ ;
- e. Arterial Dispersion time (ADT) =  $\sigma_1 \sqrt{1 + \alpha_1}$ ;
- f. Tissue Dispersion Time (TDT) =  $\sigma_2 \sqrt{1 + \alpha_2}$ ;
- g. Relative Arterial Dispersion (RAD) = ADT/DT; and
- h. Relative Tissue Dispersion (RTD) = TDT/MTT.

66. (NEW) The method of claim 53, wherein said  $\text{AIF}_i(t)$  is measureable in a small lumen showing a delay relative to said  $\text{AIF}_a(t)$ , wherein optimized values for said  $\sigma_1$  and said  $t_1$  are determined by fitting said simulated  $\text{AIF}_i(t)$  to said measured  $\text{AIF}_i(t)$ , wherein said relative dispersion  $\beta_1$  is determined and applied to all other said intensity data of said ROI using said  $\beta_1$ , wherein a more robust

fitting process is provided by a reduced number of parameters for optimization.

67. (NEW) The method of claim 66, wherein when said relative dispersion  $\beta_1$  is determined, said vascular transport function  $h_a(t)$  is described by a single variable said  $t_1$  with a constant said  $\beta_1$ , wherein a two-step method is used to determine said delay and said dispersion values comprising:

- a. deriving an initial tissue impulse residue function  $R_0(t)$  by deconvolving  $C(t) = (F_0/k_H)AIF_a(t) \otimes R_0(t)$  using a model-free singular value decomposition (SVD) method, wherein said time delay  $t_1$  is determined by a maximum position of said  $R_0(t)$  at  $R_{0\max}(t=t_1)$ ; and
- b. determine said  $AIF_t(t)$  at an input of said ROI using said  $h_a(t)$  with said  $t_1$  and said  $\beta_1$  held constant, wherein said  $\sigma_1$  is determined.

68. (NEW) The method of claim 67, wherein a value of tissue blood flow  $F_t$  and a corrected impulse residue function  $R_e(t)$  are obtained by deconvolving  $C(t) = (F_t/k_H)AIF_t(t) \otimes R_e(t)$  using said SVD method, wherein said perfusion indices are determined from a curve of said  $R_e(t)$ , wherein  $MTT = \int_0^\infty R_e(\tau) d\tau$ ,  $BF = F_t$ , and  $BV = BF * MTT$ .

69. (NEW) The method of claim 53, wherein said contrast agent is in a tissue ROI having a tissue mean transit time  $\tau$ , wherein a tissue impulse residue function is approximated by the relation  $R(t > \tau) = Ee^{-k(t-\tau)}$  and  $R(t \leq \tau) = 1$ , wherein  $E$  is an extraction fraction of said contrast agent in said tissue, wherein  $k$  is a constant

clearance rate of said contrast agent diffusing from said tissue having a relation  $k = E \cdot F_t / V_e$ , wherein  $V_e$  is the volume fraction of extravascular and extracellular space (EES) in said tissue.

- 5            70. (NEW) The method of claim 69, wherein said tissue impulse residue  
function  $R_s(t)$  of said simulated concentration curve  $C_s(t)$  is replaced by an  
average impulse residue function that incorporates said contrast agent  
leaked out of a blood vessel into said tissue and gradually clearing from  
said tissue, wherein said simulated concentration curve  $C_s(t)$  is fitted to said  
10            measured  $C(t)$  and quantitative said blood perfusion indices are calculated,  
wherein said  $E$  and said  $V_e$  are additional parameters optimized with other  
adjustable parameters using a least squares method.